

specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Finally, the Examiner states that the application fails to comply with the requirements of 37 C.F.R. §§1.821-1.825.

This Response addresses each of the Examiner's rejections and objections. Applicants therefore respectfully submit that the present application is in condition for allowance. Favorable consideration of all pending claims is therefore respectfully requested.

With respect to the requirement under 37 C.F.R. §§1.821-1.825, the Examiner points out that the nucleotide and amino acid sequences in Figure-1, 8 and 9 are not identified by sequence identifiers.

Applicants have amended the specification to insert the references to certain sequence identifiers in the description of Figure-1, 8 and 9. In addition, Applicants have added in the Sequence Listing the sequences of SEQ ID NOS: 10-15, which are disclosed in Figure-1, 8 and 9 as originally filed. A substitute paper copy and a substitute computer readable copy of the Sequence Listing are also enclosed, along with a statement under 37 C.F.R. §1.821(f) verifying the identity of the contents of these copies. As such, Applicants respectfully submit that the present application fully complies with the requirements under 37 C.F.R. §§1.821-1.825.

With regard to the new matter rejection under §312, the objection to the substitute drawings and the rejection of claims 21-24 under §112, first paragraph, these rejections and objection appear to be raised on a common ground and will be addressed together.

In the first instance, it is observed that claims 21-22 are drawn to isolated nucleic acid molecules which encode the amino acid sequences of SEQ ID NO: 7 and 9, respectively. Claims 23-24 are drawn to isolated nucleic acid molecules comprising the nucleotide sequences of SEQ

ID NO: 6 and 8, respectively. By way of the amendment filed on January 23, 2002, Applicants amended the nucleotide sequences of SEQ ID NO: 6 and 8, and the amino acid sequences of SEQ ID NO: 7 and 9. The corresponding drawings were also amended.

The Examiner states that the changes to the nucleotide sequences of SEQ ID NO: 6 and 8 and to the amino acid sequences of SEQ ID NO: 7 and 9 are not supported WO97/35971 (PCT/AU97/00199, filed 03/27/97) and the Australian priority document PN8965 filed 03/27/96. The Examiner further states that Applicants have not pointed out where in Figures 1 and 8 of the instant specification, or where in Figures 9A and 9B of PN8965, there is support for the changes made in the sequences. The Examiner points out that Figures 9A and 9B of WO97/35971 are not identical to Figures 9A and 9B of PN8965. Furthermore, the Examiner points out that Figures 9A and 9B of WO97/35971 set forth amino acid sequences, whereas Figures 9A (636bp) and 9B (808bp) of PN8965 set forth nucleotide sequences. In addition, the Examiner states that the instant specification fails to incorporate the priority document (PN8965) by reference. The Examiner contends that there is no evidence that any information omitted from this application was intended to be included in the instant application at the time of filing. Therefore, the recent amendment in the SEQ ID NO(s) is considered to be a new matter, which cannot be supported by PN8965.

→ Applicants respectfully submit that the amendment filed on January 23, 2002 sought to correct two clerical errors in the protein sequence of SEQ ID NO: 7 at positions 101 and 135. SEQ ID NO: 7 as amended, i.e., the correct sequence of the human Bcl-w protein, is the same as the "Bcl-w" sequence depicted in Figure 8 of the instant application as originally filed. Therefore, it is respectfully submitted the amendment to the sequence of SEQ ID NO: 7 is supported by the instant application as originally filed.

Applicants further submit that the amendment filed on January 23, 2002 also sought to correct certain clerical errors in the protein sequence of SEQ ID NO: 9. SEQ ID NO: 9 as amended, i.e., the correct sequence of the murine Bcl-w protein, is exactly the same as the "Bcl-w" sequence depicted in Figure 1 of the instant application as originally filed. Therefore, it is respectfully submitted the amendment to the sequence of SEQ ID NO: 9 is supported by the instant application as originally filed.

Further, Applicants respectfully submit that the amendment filed on January 23, 2002 also sought to correct two typographical errors in the nucleotide sequence of SEQ ID NO: 6 (human bcl-w) at nucleotide position 301, 404 and 405, as well as certain typographical errors in the nucleotide sequence of SEQ ID NO: 8 (murine bcl-w). These changes were clearly indicated in the marked-up copy of the amended Sequence Listing filed on January 23, 2002. SEQ ID NO: 6 and SEQ ID NO: 8 as amended, i.e., the correct human and murine bcl-w nucleotide sequences are the same as the nucleotide sequences as depicted in Figure 9A and 9B, respectively, of the priority document, Australian Provisional Application PN8965, filed on March 27, 1996. A copy of the priority document was provided to the Examiner together with the amendment filed on January 23, 2002. Therefore, Applicants respectfully submit that the amendment to SEQ ID NO: 6 and SEQ ID NO: 8 was intended to correct errors that are clerical in nature.

Applicants further respectfully submit that the originally filed Figures 9A to 9B(iv), which set forth the nucleotide and protein sequences of human bcl-w and murine bcl-w, contain the same typographical errors as the original Sequence Listing. Accordingly, by way of the amendment filed on January 23, 2002, Applicants provided substitute sheets of Figures 9A and 9B. The substitute drawing of Figure 9A discloses the nucleotide sequence (SEQ ID NO: 6) and the encoded protein sequence (SEQ ID NO: 7) of human bcl-w. The substitute drawing of

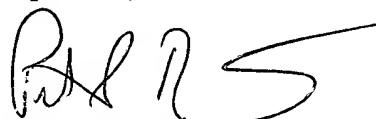
Figure 9B discloses the nucleotide sequence (SEQ ID NO: 8) and the encoded protein sequence (SEQ ID NO: 9) of murine bcl-w. These substitute sheets of drawings do not introduce new matter and are fully supported by the application as filed and by the priority document.

In view of the foregoing, it is respectfully submitted that the rejection under §132, the objection to the drawings and the rejection under §112, first paragraph, are overcome. Withdrawal of the rejections and the objection to the drawings is respectfully requested.

Attached hereto is a marked-up version of the changes made to the specification by the instant amendment. The attached page is captioned "**Version with Markings to Show Changes Made.**"

In view of the foregoing amendments and remarks, it is firmly believed that the subject application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,



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Enclosures:

- Marked up version of the amendment to the specification;
- **Exhibit A** (sequences added to the Sequence Listing);
- Substitute paper and computer-readable copy of the Sequence Listing
- Statement under §1.821(f)

Serial No: 09/155,327

**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

**IN THE SEQUENCE LISTING:**

The Sequence Listing has been amended to add sequences identified by SEQ ID NOS: 10-15, respectively. The added sequences are set forth in the sheets attached hereto as Exhibit A.

**IN THE SPECIFICATION:**

Please replace the paragraph beginning at page 24, line 13 with the following paragraph:

--**Figure 1** is a representation showing predicted amino acid sequences encoded by murine *bcl-w* cDNAs (top line, "Bcl-w", SEQ ID NO: 9) and chimaeric cDNAs corresponding to transcripts spliced from exon 3 of the *bcl-w* gene to an exon of the adjacent *rox* gene (bottom line, "Bcl-w-Rox", SEQ ID NO: 10). Boxes highlight the regions of highest homology within the Bcl-2 family, denoted S1, S2 and S3 (Cory, 1995). The arrowhead marks the position corresponding to an intron within the gene. Two residues that differ in human Bcl-w are indicated above the mouse sequence. Not all of the *rox* cDNA sequences was determined in both orientations.--

Please replace the paragraph beginning at page 26, line 20 with the following paragraph:

--**Figure 8** is a representation of a comparison of survival and anti-survival Bcl-2 sub-families. Human Bcl-2 (SEQ ID NO: 11), Bcl-x<sub>L</sub> (SEQ ID NO: 12), Bcl-w (SEQ ID NO: 7), Bax (SEQ ID NO: 13) and Bak (SEQ ID NO: 14) amino acid sequences were aligned by the Wisconsin PILEUP program. The most conserved portion of the Ced 9 sequence (SEQ ID NO:

15) and a short conserved segment in Bik are also shown. Gaps made in individual sequences to optimise alignment are indicated by dots. Residues identical or very similar (L ~ M; E ~ D; K ~ R; V ~ I) in the survival-promoting proteins Bcl-2, Bcl-x<sub>L</sub> and Bcl-w are shown on a black background, as are also those identical or very similar in all the Bcl-2 homologues. A grey background indicates residues shared by Bak and Bax but not present in the survival proteins. Homology regions S1, S2 and S3 (Cory , 1995) and the hydrophobic C-terminal segment are boxed, while the BH1, BH2, BH3 and NH1 regions defined by others (Yin *et al.*, 1994; Subramanian *et al.*, 1995) are overlined. Filled arrowheads indicate conserved residues specific to the survival proteins; open arrowheads, those specific to anti-survival proteins. An unbroken arrow indicates the position of the splice site common to all the proteins; a broken arrow, the position of the alternative 5' splice that creates the smaller Bcl-x protein and a wavy line a conserved C-terminal motif.--

Please replace the paragraph beginning at page 27, line 6 with the following paragraph:

--**Figure 9** is a representation of the coding region of (A) human (SEQ ID NO: 6) and (B) murine (SEQ ID NO: 8) *bcl-w*.--